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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,868	09/06/2006	Shouming Wang	6613-76359-01	4672

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EXAMINER

HA, JULIE

ART UNIT	PAPER NUMBER
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1654

MAIL DATE	DELIVERY MODE
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10/15/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/591,868	Applicant(s) WANG, SHOUMING	
	Examiner JULIE HA	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on June 19, 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5, 7, 15-22 and 26-41 is/are pending in the application.
- 4a) Of the above claim(s) 3, 4, 26-28 and 41 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 5, 7, 15-22 and 29-40 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to Election/Restriction filed on June 19, 2008 is acknowledged. Claims 6, 8-14, 23-25 have been cancelled and new claims 29-41 have been added. Claims 1-5, 7, 15-22, 26-41 are pending in this application.

Restriction

1. Applicant's election of Group I (claims 1-5, 7 and 15-22) and the election of species Cbz-(R)-4-F-Phe-(S)-Pro-(R)-boroMpg-OH with sodium as the counter-ion (TRI 50f) in the reply filed on June 19, 2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. The restriction requirement is deemed proper and is made FINAL in this office action. Claims 26-28 and 41 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 3 and 4 are withdrawn from further consideration, as being drawn to nonelected species. For example, the elected species has on halogenated 6-membered ring, therefore, E, E¹, E², E³ cannot be independently a halogenated 6-membered ring. Claims 1-2, 5, 7, 15-22 and 29-40 are examined on the merits in this office action.

Rejection

35 U.S.C. 112, 2nd

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-2, 5, 7, 15-22, 29, 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites, "aa² is a residue of an amino acid which binds to the thrombin S2 subsite..." It is unclear what is encompassed by the claim recitation. It is unclear what residue of an amino acid would bind to the thrombin S2 subsite. Furthermore, it is unclear what "residue" of an amino acid is. For example, a residue of an amino acid may be part of an amino acid or a residue left over from other components (such as resin) when the peptide is being synthesized. The dictionary.com defines residue as "something that remains after a part is removed, disposed of, or used; remainder; rest; remnant" and "an atom or group of atoms considered as a group or part of a molecule; that part remaining as a solid on a filter paper after a liquid passes through in the filtration procedure." Because claims 2, 5, 7, 15-22, 29 and 32-34 depend from indefinite claim 1 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

5. Claims 29-34 recites the limitation "R¹" in claims 29 and 32-33. There is insufficient antecedent basis for this limitation in the claims. Claim 29 is dependent on claim 1, which recites a compound having formula (I), and the variables recited are X,

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aa¹, aa², R⁹, a, b, c, d, E, E¹, E², E³, m, and W. The variable R¹ is never recited in claim

1. The first time R¹ is recited is in claim 29. Therefore, claims 29-34 lack antecedent basis.

35 U.S.C. 112, 1st

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-2, 5, 7, 15-22, 29-30, 32-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties,

functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient.” MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

“A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; In re Smythe, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative

number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. In re Gostelli, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a compound selected from boronic acids of formula (I) and pharmaceutically acceptable salts, wherein aa² is a residue of an amino acid which binds to the thrombin S2 subsite. The generic statement residue of an amino acid does not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable claim 1 is broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of peptide or a peptide-like molecule that can from an amide bond or peptide linkage and any class of amino acid or amino acid mimetics that can from an amide bond, or any class of compounds that are residues of a component. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is “not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.” MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds

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beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules, other amino acid mimetics, and other synthetic peptide or peptide-like molecule that can function as a residue of an amino acid or a residue of an amino acid.

The specification discloses that aa² is a residue of an amino acid which binds to the thrombin S2 subsite (see paragraphs [0131] and [0518] of instant specification US 2007/0185060 A1). The specification does not disclose what residues bind to the S2 subsite of thrombin. The specification discloses a functional characteristic of the residue of aa²; that is binds to S2 subsite of thrombin. The working example describes the protein gelatin being crosslinked (see paragraph [0049]). All of the working examples describe synthesis of boronic peptide wherein the aa² is a proline amino acid residue. None of the working examples describe a residue of an amino acid that are mimetics or variants of amino acids, nor any residual components left over from synthesis of the boronic peptide, such as resin particles (residue), etc. The working example only describes aa² having the formula (IV), that is proline amino acid residue. Again, the specification does not describe any other residues of amino acids or amino acid residues that bind to the S2 subsite of thrombin. Description of proline is not sufficient to encompass numerous other synthesis components and other amino acid residues that

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belong to the same genus. For example, there are varying amino acid residues that may bind to the S2 subsite of thrombin, varying amino acid compositions, and numerous distinct qualities that make up the genus. Furthermore, there are amino acid mimetics and non-natural amino acid that mimic the natural amino acids and function the same way. For example, there are D-isomers, β -amino acid, γ -amino acid, ϵ -amino acid, protected amino acid, that belong to the same genus, and function the same way. Additionally, applying the broadest reasonable interpretation to the claim language "residue of an amino acid", the residue may also be a residue that is cleaved off the resin after the completion of the synthesis. Since the word "residue" is unclear, this may be any component that is attached to the amino acid. Therefore, there is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention.

See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984)

(affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Rejection-35 U.S.C. 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

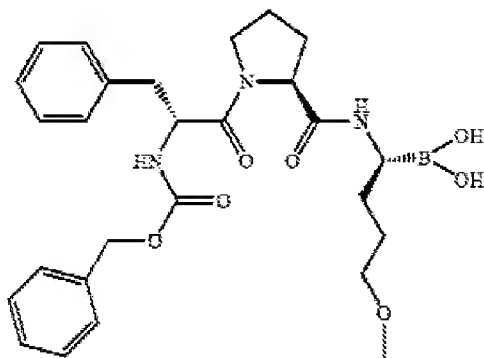
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1-2, 5, 7, 15-22 and 29-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Deadman et al (US Patent No. 7,112,572) in view of O'Hagan et al (Chemical Communications, 1997, 645-652).

11. Deadman et al teach salts of a pharmaceutically acceptable divalent metal and an organoboronic acid drugs (see abstract). Deadman teaches a TRI-50c compound

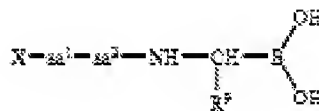


having the structure

and name Cbz-(R)-Phe-(S)-

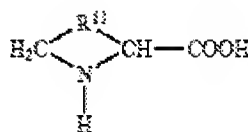
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Pro-(R)-boroMpg-OH (see Example 3). Since the R⁹ is methoxypropyl and X is benzyloxycarbonyl (Cbz), this meets the limitation of claims 31-34. Furthermore,



Deadman teaches the compound of formula (IV): , wherein X

is a moiety bonded to the N-terminal amino group and may be H to from NH₂...can be benzyloxycarbonyl (Cbz), aa¹ is an amino acid residue having a hydrocarbly side chain containing no more than 20 carbon atoms and comprising at least one cyclic group



having up to 13 carbon atoms, and formula (V): for aa² residue

(see columns 24-25), meeting the limitation of claims 1-2, 5, 29-40, in part. The reference teaches that the formulation is administered intravenously or subcutaneously (see column 17), meeting the limitation of claims 20 and 21. Further, the reference teaches that oral administration of TRI 50c (see column 33), meeting the limitation of claims 20 and 22. Deadman further teaches that the compound is salt of boronic acid (organoboronic acid drug) (see abstract), this meets the limitation of claim 15.

Additionally, the reference teaches that the salt of the peptide boronic acid is with an alkali metal salts of TRI 50c (see column 38) which is a TRI 50c sodium salt (see Example 10), and comprises boronate ions (see claim 10), meeting the limitations of claims 16-19. The difference between the reference and the instant claims is that the reference does not teach 4-fluoro-Phe as aa¹.

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12. However, O'Hagan teaches that the van der Waals radii of fluorine lies between oxygen and hydrogen, and thus fluorine appears to have a particularly close isosteric relationship to oxygen while being larger than hydrogen. However, in solid state X-ray structures, fluorine and hydrogen often interchange, and scanning tunneling microscopy analyses of monofluorinated stearic acids deposited on graphite shows very little distortion in two dimensional packaging, suggesting a very close isosteric relationship between hydrogen and fluorine. Consistent with this, the steric impact of replacing hydrogen by fluorine is never too great and binding of analogues to target proteins is not normally impeded. Thus, despite the size anomaly, fluorine emerges as a reasonable hydrogen mimic.

13. Therefore, it would have been obvious to one of ordinary skill in the art to substitute a hydrogen with a fluorine. The MPEP states the following: "Prior art structures do not have to be true homologs or isomers to render structurally similar compounds prima facie obvious. In re Payne, 606 F.2d 303, 203 USPQ 245 (CCPA 1979) (Claimed and prior art compounds were both directed to heterocyclic carbamoyloximino compounds having pesticidal activity. The only structural difference between the claimed and prior art compounds was that the ring structures of the claimed compounds had two carbon atoms between two sulfur atoms whereas the prior structure had either one or three carbon atoms between two sulfur atoms. The court held that although the prior art compounds were not true homologs or isomers of the claimed compounds, the similarity between the chemical structures and properties is sufficiently close that one of ordinary skill in the art would have been motivated to make

the claimed compounds in searching for new pesticides.)” See MPEP 2144.09. One of ordinary skill in the art would have been motivated to substitute a fluorine for a hydrogen, since fluorine acts as a hydrogen mimic. Furthermore, fluorine is more stereoelectronic than hydrogen, therefore, it would behave better in a less polar environment, such as the enzyme environment. There is a reasonable expectation of success, since fluorine does not give a steric impact, and acts as a hydrogen mimic, one would at least expect that the fluorine substituted compound would at least act similarly to the compound having a hydrogen. The type of fluorine substitution for a hydrogen is deemed merely a matter of judicious selection and routine optimization that is well within the purview of skilled artisan.

Obviousness Double Patenting

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

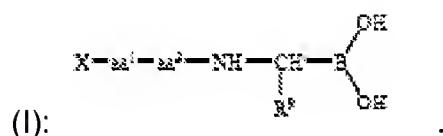
15. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

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16. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

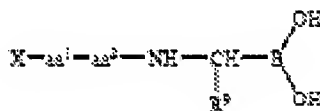
17. Claims 1-2, 5, 7, 15-22, 29-40 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-18 of copending Application No. 10/591,962 (US 2008/0166396 A1) in view of O'Hagan et al (Chemical Communications, 1997, 645-652).

18. Instant claims are drawn to a compound of boronic acids of formula



19. The copending claims are drawn to an oral pharmaceutical dosage form

comprising boronic acids of formula (III) and salts thereof.



The difference between the reference and the instant claims is that the reference does not teach a 4-F-Phe for aa¹.

20. However, O'Hagan teaches that the van der Waals radii of fluorine lies between oxygen and hydrogen, and thus fluorine appears to have a particularly close isosteric relationship to oxygen while being larger than hydrogen. However, in solid state X-ray structures, fluorine and hydrogen often interchange, and scanning tunneling microscopy analyses of monofluorinated stearic acids deposited on graphite shows very little distortion in two dimensional packaging, suggesting a very close isosteric relationship between hydrogen and fluorine. Consistent with this, the steric impact of replacing hydrogen by fluorine is never too great and binding of analogues to target proteins is not

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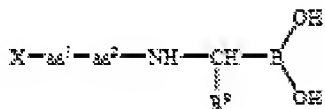
normally impeded. Thus, despite the size anomaly, fluorine emerges as a reasonable hydrogen mimic.

21. Therefore, if one of ordinary skill in the art practiced the claimed invention of co-pending application in view of O'Hagan et al, then one would necessarily lead to the claimed invention of the instant claims, and vice versa. One of ordinary skill in the art would be motivated to substitute a fluorine for a hydrogen, since fluorine is a hydrogen mimic and the electronegativity of the fluorine would react better in vivo, in the physiological environment of the enzyme. There is a reasonable expectation of success, since fluorine is a reasonable hydrogen mimic, since it does not impact steric hindrance, and one would at least expect at least a similar acting compound.

This is a provisional obviousness-type double patenting rejection.

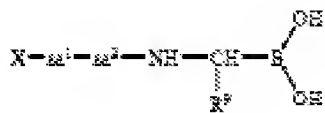
22. Claims 1-2, 5, 7, 15-22, 29-40 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 12-20, 23-24, 26-34, 50 and 55-56 of U.S. Patent No. 7,112,572 in view of O'Hagan et al (Chemical Communications, 1997, 645-652).

23. The instant claims are drawn to a compound selected from boronic acids of



formula (I):

24. The claims of US Patent No. 7,112,572 are drawn to a slat of a pharmaceutically acceptable multivalent meal and an organoboronic acid inhibitor of thrombin having



formula (IV): , a medicament comprising the boronic peptide of formula (IV), and a pharmaceutical formulation comprising boronic peptide of formula (IV). The difference between the reference and the instant claims is that the reference does not teach 4-F-Phe for aa¹.

25. However, O'Hagan teaches that the van der Waals radii of fluorine lies between oxygen and hydrogen, and thus fluorine appears to have a particularly close isosteric relationship to oxygen while being larger than hydrogen. However, in solid state X-ray structures, fluorine and hydrogen often interchange, and scanning tunneling microscopy analyses of monofluorinated stearic acids deposited on graphite shows very little distortion in two dimensional packaging, suggesting a very close isosteric relationship between hydrogen and fluorine. Consistent with this, the steric impact of replacing hydrogen by fluorine is never too great and binding of analogues to target proteins is not normally impeded. Thus, despite the size anomaly, fluorine emerges as a reasonable hydrogen mimic.

26. Therefore, if one of ordinary skill in the art practiced the claimed invention of co-pending application in view of O'Hagan et al, then one would necessarily lead to the claimed invention of the instant claims, and vice versa. One of ordinary skill in the art would be motivated to substitute a fluorine for a hydrogen, since fluorine is a hydrogen mimic and the electronegativity of the fluorine would react better in vivo, in the physiological environment of the enzyme. There is a reasonable expectation of success,

since fluorine is a reasonable hydrogen mimic, since it does not impact steric hindrance, and one would at least expect at least a similar acting compound.

Conclusion

27. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/

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Primary Examiner, Art Unit 1654

/J. H./
Examiner, Art Unit 1654